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Organic Acid and Amino Acid Testing Masterclass

OMX Metabolomics in Clinical Practice

Presenter:

Dr Oscar Coetzee

Host: Lea McIntyre

Our Panel

Presenter | Dr Oscar Coetzee, Clinical Nutritionist, Associate Professor

Motivated by his desire to reverse the chronic illness epidemic, Dr Coetzee continues to be a pioneer in the field of nutritional science.
Born and raised in South Africa, where he completed his military schooling and earned bachelor's degrees in criminology and psychology, Dr Coetzee also earned a masters degree in Human Nutrition from University of Bridgeport (USA).
He went on to receive a PhD in holistic nutrition from Clayton College of New Hampshire (USA), and a Doctorate of Clinical Nutrition (DCN). Dr Coetzee finished his second doctorate from Maryland University of Integrative Health, with a specialisation in nutrigenomics.
His key areas of interest are metabolic syndrome, intestinal permeability, type 2 diabetes, sports performance, and most chronic inflammatory diseases.

Host | Lea McIntyre ND

Lea McIntyre is Technical Marketing Manager at Designs for Health Australia.
She has 20 years experience as a qualified naturopath, herbalist and nutritionist.
In her clinical practice, she has a special interest in paediatric health and gut health and the relationship between inflammation and neurological conditions.

OMX™

ORGANIC METABOLOMICS

Designs for Health, Australia have partnered with Diagnostic Solutions Lab to exclusively distribute the OMX test in Australia.

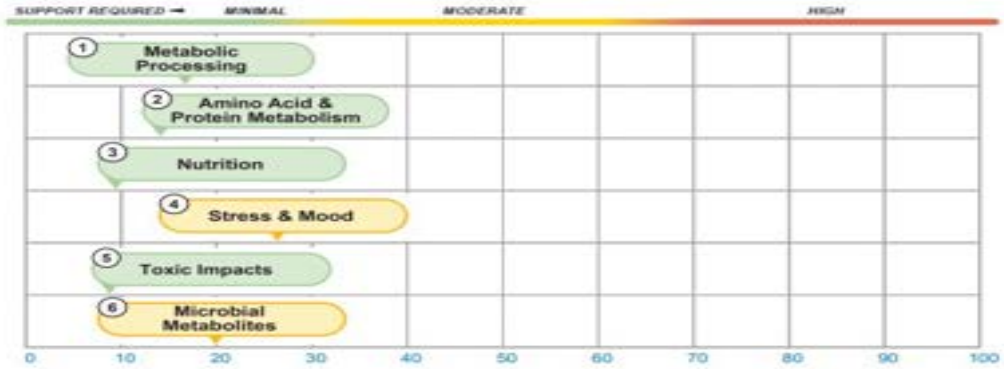
For further information, you can visit our Fx Testing page after signing in at https://designsforhealth.com.au/fx-testing/ for more information, or by calling 02 9136 6266 and speaking with customer service.

CASE STUDY

Case Study – Marie – Overview

METABOLOMIC SIGNATURE

Identifying Impact of Functional Categories



Findings show that 2 of 6 Functional Categories have markers beyond the reference range.

Subcategories are identified below.

Identifying Impact of Subcategories

NOTE: Below is a list of the Functional Categories and the included subcategories. It lists the percentage of markers that are beyond the reference range so clinicians can better target areas of concern.

PERCENT OF MARKERS BEYOND THE REFERENCE RANGE

0-20%	21-60%	61-100%
MINIMAL	MODERATE	HIGH

1 Metabolic Processing — 19 %

Subcategory
- Glycolysis
- Krebs Cycle
- Fatty Acid Oxidation
- Ketones

2 Amino Acid & Protein Metabolism — 11 %

Subcategory
- Phenylalanine Metabolism
- Branched-Chain Amino Acids
- Tryptophan Metabolism
- Methionine Metabolism
- Histidine Metabolism
- Threonine/Glycine/Serine
- Lysine Metabolism
- Glutamate & Aspartate
- Collagen Catabolism

3 Nutrition — 7 %

Subcategory
- B-Complex (B1, B2, B3, B5, LA)
- Vitamin B-12
- Folate
- Vitamin B6
- Biotin
- Plant Components
- Meat intake
- Sugar Intake

4 Stress & Mood — 29 %

Subcategory
- Neurotransmitter
- Catecholamine Turnover
- Serotonin Turnover
- Steroid Hormone

5 Toxic Impacts — 7 %

Subcategory
- Oxidative Damage
- Toxins
- Urea Cycle
- Kidney Impacts

6 Microbial Metabolites — 22 %

Subcategory
- Amino Acid Microbial Metabolites
- Polyphenols Microbial Metabolites
- Isoflavone microbial Metabolites
- Fungal Assessment

CASE STUDY

Marie – Metabolic Processing Panel

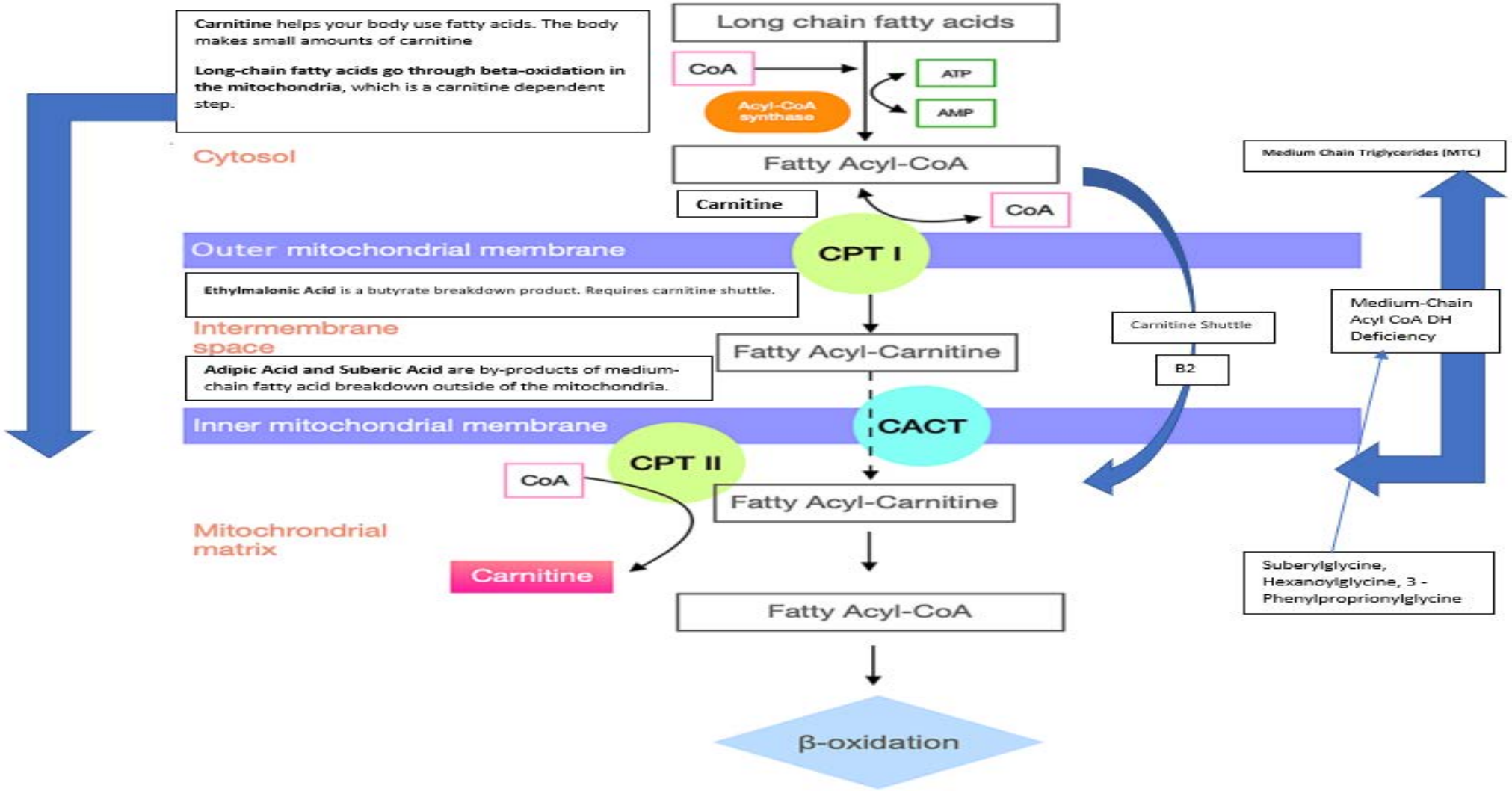
1 - Metabolic Processing

Fatty Acid Oxidation	Result	Reference
Adipic Acid *Saturated dicarboxylic acid*	22.4 H	2.0 - 15.1 nmol/mg Creatinine
Sebacic Acid *Fatty acid oxidation + Carnitine*	9.2 H	< 3.7 nmol/mg Creatinine
Suberic Acid *Fatty acid oxidation + Carnitine*	30.7 H	3.0 - 29.4 nmol/mg Creatinine
Pimelic Acid *Saturated dicarboxylic acids*	38.5 H	5.9 - 31.8 nmol/mg Creatinine
Hexanoylglycine *Medium-chain acyl glycines*	0.5	< 2.6 nmol/mg Creatinine
Suberylglycine *Medium-chain acyl glycines*	<DL	< 2.3 nmol/mg Creatinine
3-Phenylpropionylglycine *Medium-chain acyl glycines*	0.5	< 1.3 nmol/mg Creatinine
Ethylmalonic Acid *Dicarboxylic acid*	16.0	5.0 - 43.3 nmol/mg Creatinine
2-Methylsuccinic Acid *Dicarboxylic acid*	11.2	3.2 - 21.1 nmol/mg Creatinine

Ketones	Result	Reference
β-Hydroxybutyric Acid *beta-Hydroxybutyrate dehydrogenase + B3*	20.4	< 60.5 nmol/mg Creatinine

CASE STUDY

OMX - Beta Oxidation Chart



Adipic Acid

- Slightly elevated adipic acid may result from excessive ingestion of gelatin or other "junk" food containing adipic acid as an additive.
- Adipic acid is naturally found in beets and sugar cane.
- Adipic acid is commonly added as the main acid in bottled drinks, giving them a bubbly fizz.
- Adds a tart flavor to fruit juice and gelatin.
- The organic acid is used in many powdered food and drink mixes to provide a sweet flavor.

- Elevated adipic acid may also indicate an abnormality in fatty acid metabolism.
- Dietary supplements containing L-carnitine or L-acetyl-carnitine may be beneficial.
- People with metabolic syndrome or diabetes had significantly elevated adipic acid, suberic acid, lactic acid, and fumaric acid.
- Ketosis is sometimes accompanied by excessive excretion of adipic and suberic acid.

CASE STUDY

Sebacic Acid

- Sebacic Acid is a urinary metabolite that has been identified as an anti-fatigue biomarker.
- Increased intake with or supplementation of medium-chain triglycerides. Those can be found in coconut or palm oils for example. Increased consumption of gelatin, jello or custards.
- Vitamin B2 (aka Riboflavin) deficiency. Riboflavin is needed for fatty acid breakdown.
- Diabetes
- Genetic disorder such as MTC acyl-CoA dehydrogenase deficiency (very elevated values might point to this). MCAD
- Other rare inherited disorders such as adrenoleukodystrophy and Zellweger syndrome.

CASE STUDY

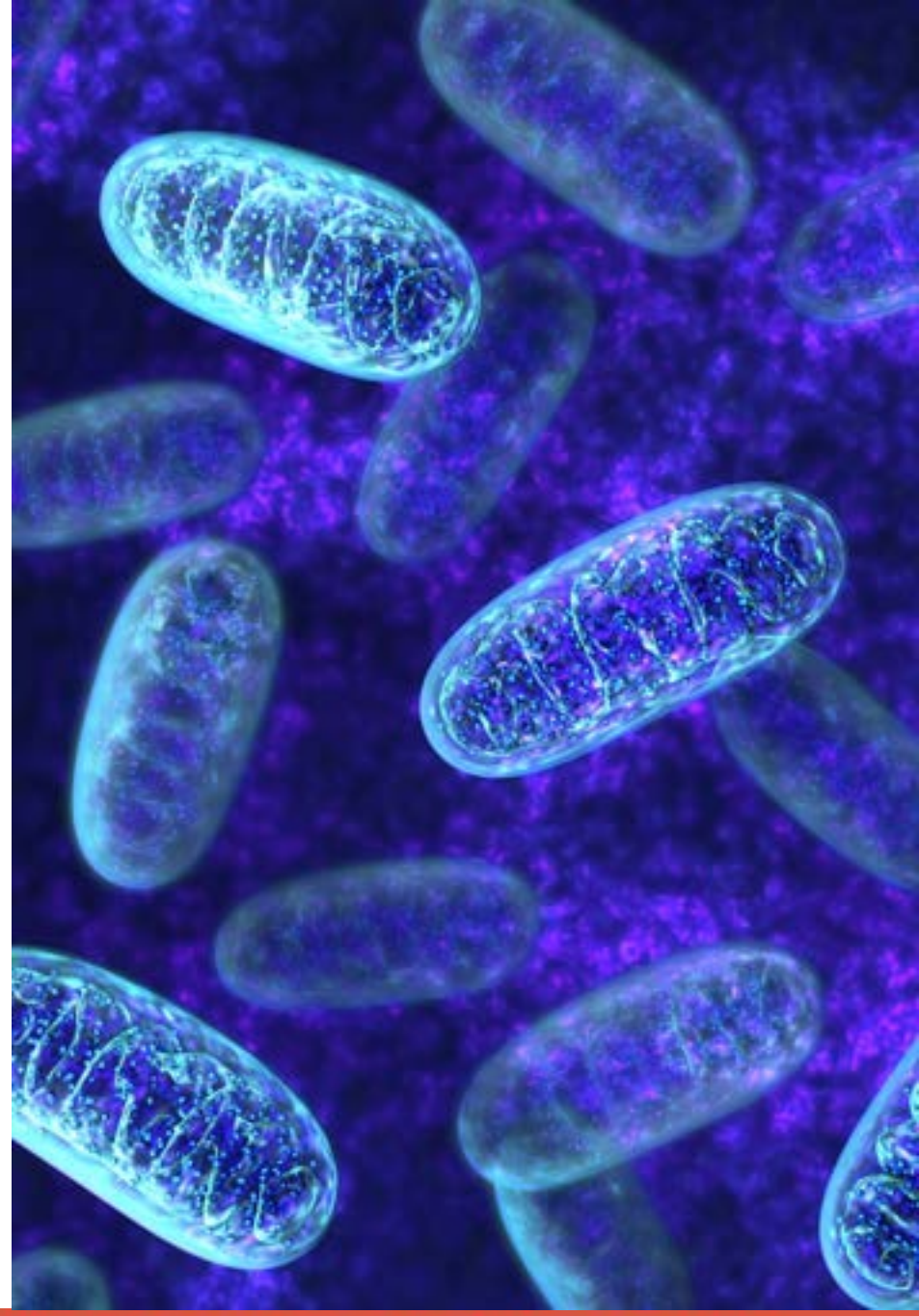
Suberic Acid

- Suberic acid is present in the urine of patients with fatty acid oxidation disorders.
- A metabolic breakdown product derived from oleic acid.
- Elevated levels of this unsaturated dicarboxylic acid are found in individuals with medium-chain acyl-CoA dehydrogenase deficiency (MCAD).
- Elevated in Schizophrenics
- People with metabolic syndrome or diabetes had significantly elevated adipic acid, suberic acid, lactic acid, and fumaric acid.
- Ketosis is sometimes accompanied by excessive excretion of adipic and suberic acid.

CASE STUDY

Pimelic Acid

- Pimelic acids are excreted in elevated amounts in urine in disorders of mitochondrial beta-oxidation and disorders of peroxisomal beta-oxidation, for which they are of significant diagnostic value.
- Pimelic acid originating from fatty acid synthesis pathway is a bona fide precursor of biotin in B. subtilis.



CASE STUDY

Marie – Amino Acid & Protein Metabolism Panel

2 - Amino Acid & Protein Metabolism

Methionine Metabolism	Result	20% 40% 60% 80%	Reference
Methionine *Methionine adenosyltransferase*	10.6		< 11.0 nmol/mg Creatinine
Homocystine *Methionine synthase + B12*	<DL		< 5.7 nmol/mg Creatinine
Cystathionine *Cystathionine gamma-lyase + B6*	46.9		3.6 - 85.5 nmol/mg Creatinine
Sulfocysteine *Sulfite oxidase (SOX) + Mo*	7.1		< 8.8 nmol/mg Creatinine
Taurine *Hypotaurine dehydrogenase*	944.6		41.9 - 3644.8 nmol/mg Creatinine
Cystine *Oxidation*	24.2		9.7 - 96.1 nmol/mg Creatinine
α-Hydroxybutyric Acid *Dehydrogenase + B3*	38.2		10.6 - 62.6 nmol/mg Creatinine
α-Ketobutyric Acid *Lactate dehydrogenase + B3*	27.5 H		< 7.2 nmol/mg Creatinine
Pyroglutamic Acid *5-Oxoprolinase*	139.0 H		< 72.7 nmol/mg Creatinine

Histidine Metabolism	Result	20% 40% 60% 80%	Reference
Histidine *Histidine decarboxylase + B6*	463.5		126.4 - 1592.8 nmol/mg Creatinine
3-Methylhistidine *Myofibrillar Breakdown*	2124.4 H		49.7 - 1852.9 nmol/mg Creatinine
β-Alanine *Carnosine synthase*	4.5		< 11.8 nmol/mg Creatinine

a-Ketobutyric Acid (Alpha-Ketobutyrate):

- Alpha-ketobutyric acid results from the breakdown of threonine or methionine during glutathione production.
- Specifically, cystathionine is metabolized to alpha-ketobutyric acid and cysteine.
- a- ketobutyric acid enters the mitochondrial matrix and get converted to propionyl-CoA by the branched chain keto-acid dehydrogenase complex (BCKDHC) and enters the Krebs cycle at succinyl-CoA.
- Evaluate lactate and the branched chain keto acids
- Evaluate alpha-hydroxybutyric acid
- Associated Nutrients: Vitamin B3
- a -Ketobutyric acid is produced from cystine, along with hydrogen sulfide (H2S) as a by-product.
- a- Ketobutyric acid is reversibly converted to a- hydroxybutyric acid.

Pyroglutamic Acid (Pyroglutamate):

- Pyroglutamic acid is produced at the end steps of glutathione and is thought to be related to cysteine insufficiency or glycine availability.
- Pyroglutamic acid becomes elevated if cysteine is deficient when gamma-glutamyl cysteine synthase combines with cysteine to form gamma-glutamyl cysteine.
- The process of glutathione production also includes glycine
- Supplement with glutathione support; glycine, N-acetyl cysteine

- Drug-induced reversible inhibition of glutathione synthetase, such as from acetaminophen, leads to elevated pyroglutamic acid.
- Researchers noted that glutathione depletion of septic patients may be noted with higher serum levels of pyroglutamate and lower levels of erythrocyte glutathione peroxidase.

3-Methylhistidine:

- 3-Methylhistidine is synthesized in muscle myofibrillar proteins by the methylation of one histidine residue in actin and in varying amounts in myosin.
- It doesn't get reused or metabolized further.
- Urinary excretion is specific to myofibrillar breakdown, assumed to be from skeletal muscle, with lesser amounts from cardiac and smooth muscle.
- Some research has noted that 3-methylhistidine was increased by endurance exercise.
- Significant changes in meat intake can impact levels of 3-methylhistidine excretion, though relatively small changes in excretion can be noted if intake is held steady.
- Current research has recommended avoiding meat two days prior to testing to get accurate results.
- Evaluation of dietary protein intake can aid in a more accurate assessment in determining if the increase in 3-methylhistidine is due to muscle breakdown.
- Evaluate for significant changes in meat intake and anabolic medication.
- Consider B-vitamins to support methylation.
- Evaluate amino acid status and levels of activity.
- Associated Nutrients: SAMe, folate, B12, B6

Marie – Nutrition Panel

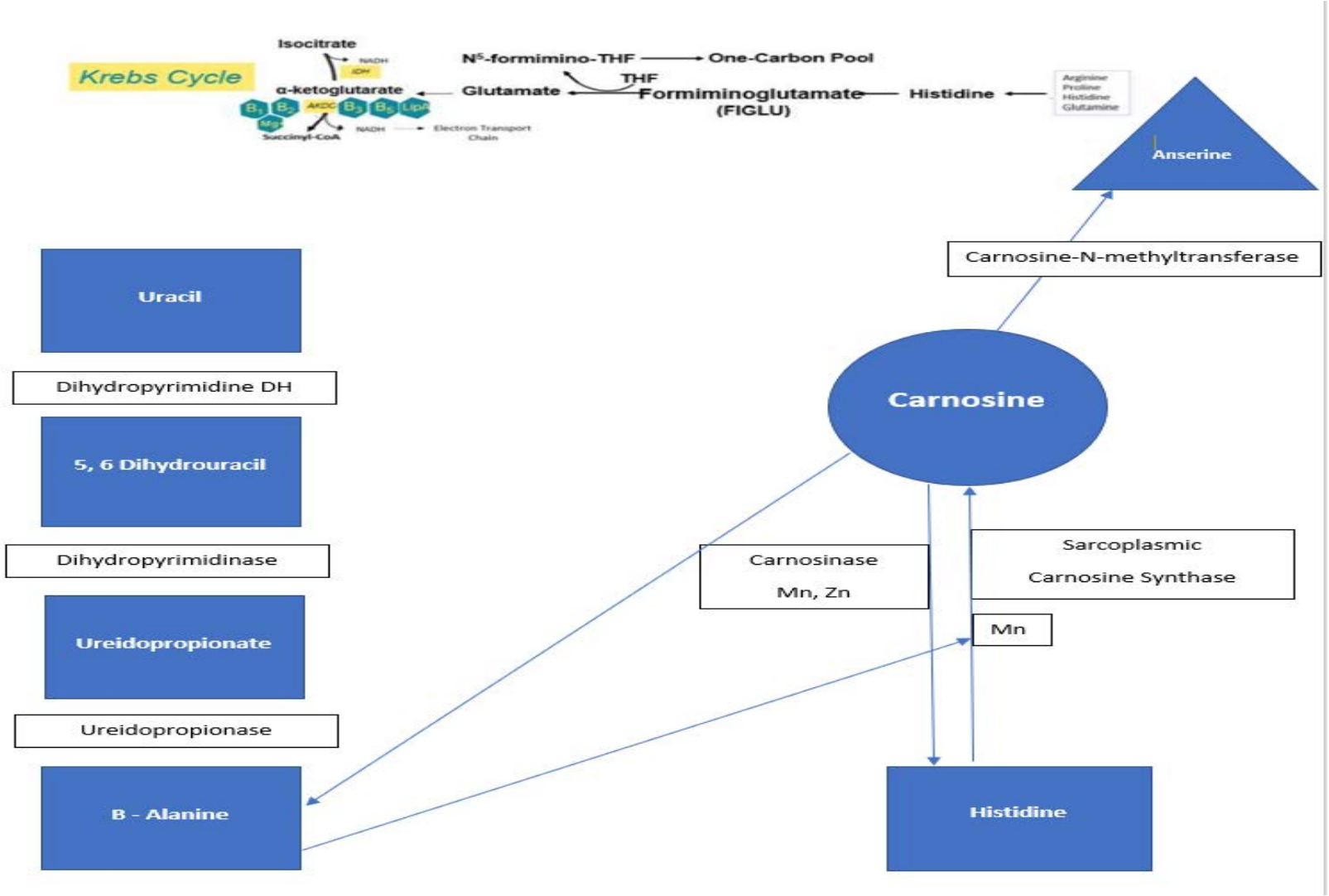
3 - Nutrition

Plant Components	Result	20% 40% 60% 80%	Reference
Quercetin *Polyphenol: Flavonoid*	5.2		> 2.7 nmol/mg Creatinine
Tartaric Acid *Plant component*	224.1		> 1.8 nmol/mg Creatinine

Meat intake	Result	20% 40% 60% 80%	Reference
1-Methylhistidine *Dietary meat & fish*	346.7		88.0 - 394.4 nmol/mg Creatinine
Carnosine *Carnosinase*	57.0		3.9 - 70.0 nmol/mg Creatinine
Anserine *Anserinase*	401.8 H		< 364.6 nmol/mg Creatinine

Sugar Intake	Result	20% 40% 60% 80%	Reference
Fructose *Fructokinase*	0.3		< 4.7 nmol/mg Creatinine

Case Study – Marie



CASE STUDY

Carnosine & Anserine:

- Carnosine is composed of beta-alanine and histidine.
- Anserine is a methylated form of carnosine.
- Both are increased in omnivore diets.
- Total meat intake was associated with plasma anserine and highest anserine concentrations were observed in individuals consuming processed meat or turkey.
- Diet is less likely to increase beta-alanine concentrations.
- Synthesis of carnosine can be impacted by multiple factors, including age, sex, muscle fiber type, muscular activity, and diet.
- Carnosine is predominantly stored within skeletal muscle.

- High serum carnosinase, the enzyme that breaks down carnosine, can limit the efficacy of carnosine supplements.
- Both carnosine and anserine have been found to have potent antioxidant properties
- Considerations:
- Evaluate dietary intake and ensure adequate protein digestion (fecal pancreatic elastase is a proteolytic enzyme used to identify overall pancreatic function).
- Correlate with dietary intake and blood level of histidine.

CASE STUDY

Marie – Stress and Mood Panel

4 - Stress & Mood

Neurotransmitter	Result	Reference
γ-Aminobutyric Acid *gamma-Aminobutyric acid aminotransferase + B6*	5.4 H	< 2.9 nmol/mg Creatinine

Catecholamine Turnover	Result	Reference
Homovanillic Acid *COMT + magnesium & monoamine oxidase + B2*	11.9 H	< 10.3 nmol/mg Creatinine
Vannilylmandelic Acid *Monoamine oxidase + B2*	15.3	4.8 - 21.4 nmol/mg Creatinine

Serotonin Turnover	Result	Reference
5-Hydroxyindoleacetic Acid *Aldehyde dehydrogenase + B3*	11.5	6.3 - 28.7 nmol/mg Creatinine

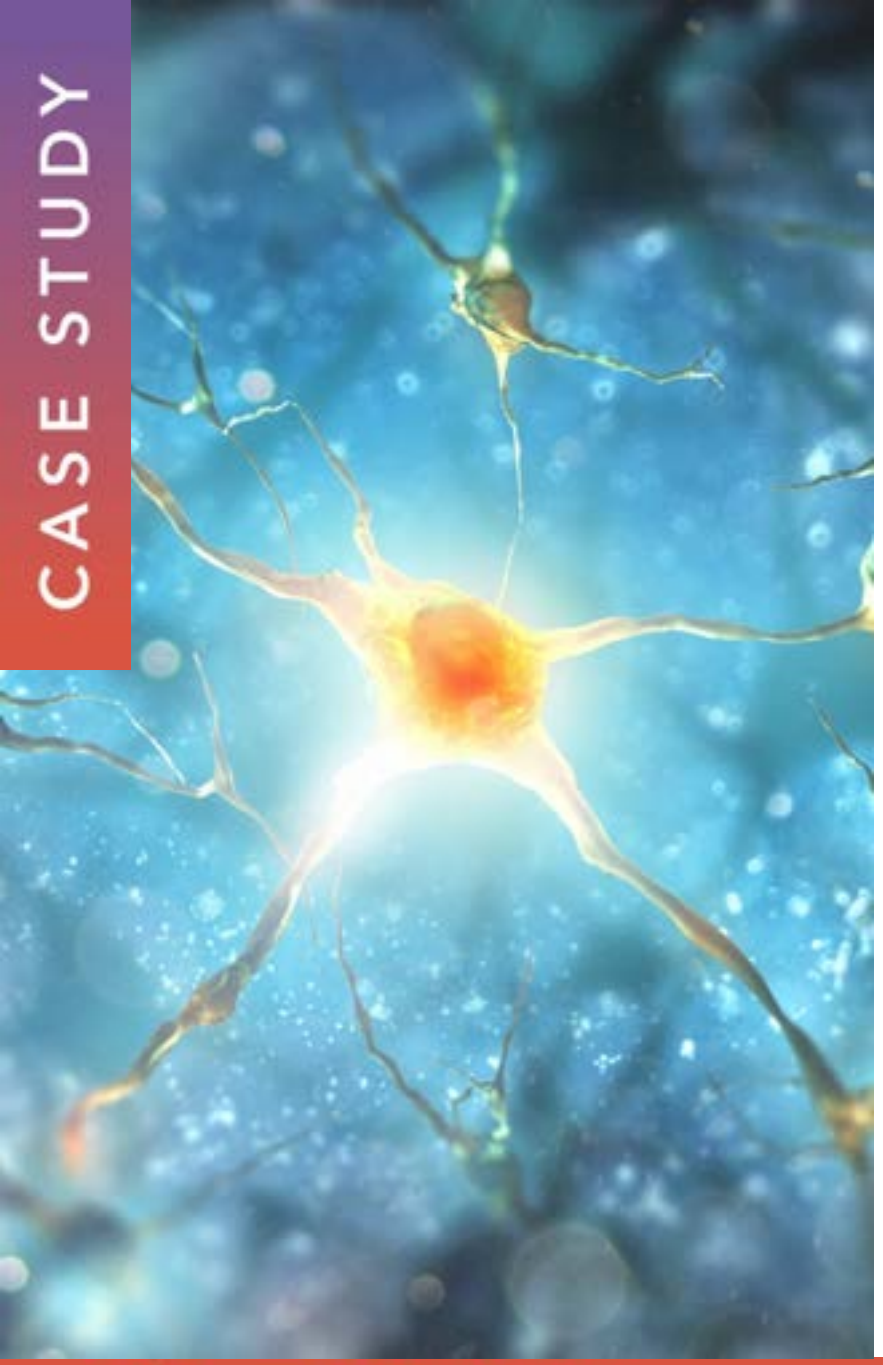
Steroid Hormone	Result	Reference
Cortisol *11-beta-Hydroxysteroid dehydrogenase + B3*	16.0	< 82.0 mcg/g Creatinine
Cortisone *11beta-hydroxysteroid dehydrogenase + B3*	38.9	< 665.0 mcg/g Creatinine
Aldosterone *Steroid 5-beta reductase*	<DL	< 2.5 mcg/g Creatinine

CASE STUDY

γ-Aminobutyric Acid Gamma Amino-Butyric Acid (GABA):

- γ-aminobutyric acid (GABA) is the main inhibitory neurotransmitter that acts in the nervous system and the immune system.
- γ-aminobutyric acid affects control of cortisol.
- Dysregulation of γ-aminobutyric acid has been associated with cognition, oxidative stress, glucose tolerance, and mood disorders.
- Foods containing γ-aminobutyric acid include tea leaves, mulberry leaves, tomato, lactic acid bacteria, yeasts and molds, fermented milk and soy products, sourdough, sprouts of brown rice, barley and beans, and kimchi, or dietary supplements.
- Pharma GABA vs GABA and the blood brain barrier (BBB)

CASE STUDY



Homovanillic Acid (HVA) (Homovanillate):

- HVA levels have shown to be related to neurotransmitter metabolism in subjects suffering from occupational stress; levels were lower in workers with higher coworker support.
- Higher scores on the Beck Depression Inventory-II, plus a decrease in the levels of plasma dopamine and urine dopamine, 3,4-dihydroxyphenylacetic acid, HVA, norepinephrine, serotonin, and hydroxyindoleacetic acid, were seen in pesticide exposed workers.
- HVA (homovanillic acid), a dopamine metabolite, and VMA (vanilmandelic acid), a metabolite of epinephrine and norepinephrine.
- May be elevated due to stress increasing catecholamine output from the adrenal gland or from lead toxicity.
- Elevated HVA may also result from the intake of L-DOPA, dopamine, phenylalanine, or tyrosine.

CASE STUDY

Marie – Toxic Impacts Panel

5 - Toxic Impacts

Toxins	Result	20% 40% 60% 80%	Reference
2-Methylhippuric Acid *Xylene exposure*	0.2		< 2.1 nmol/mg Creatinine
Mandelic Acid *Styrene exposure*	0.9		< 4.6 nmol/mg Creatinine
Benzoylform *Styrene exposure*	1.8		< 4.3 nmol/mg Creatinine
Glucaric Acid *Glucuronic Acid Pathway*	53.5 H		3.6 - 25.8 nmol/mg Creatinine

Glucaric Acid:

- Urinary glucaric acid has been used as an indicator of induced hepatic drug metabolization and elevated with exposure to xenobiotics.
- Levels may indirectly represent P-450 activity or an end-product of the glucuronidation pathway.
- Dietary glucaric acid and supplementation with calcium-D-glucarate may suppress cell proliferation and inflammation, induce apoptosis, and have anticancer properties.
- Glucaric acid from dietary plants may act as a nontoxic β-glucuronidase inhibitor.
- Vegetarians may have higher levels.
- It has been found increased with increased PCBs, toxins, and medications.

CASE STUDY

Marie – Microbial Metabolites Panel

6 - Microbial Metabolites

Amino Acid Microbial Metabolites	Result	Reference
4-Hydroxyphenylacetic Acid *Disordered tyrosine metabolism*	115.9	85.8 - 902.3 nmol/mg Creatinine
Indoleacetic Acid *Disordered tryptophan metabolism*	19.5 H	< 13.7 nmol/mg Creatinine

Polyphenols Microbial Metabolites	Result	Reference
3,4-Dihydroxyhydrocinnamic Acid *Polyphenol metabolite*	<DL	< 1490.3 nmol/mg Creatinine
3,5-Dihydroxybenzoic Acid *Microbial metabolite*	88.1	< 277.1 nmol/mg Creatinine
4-Hydroxybenzoic Acid *Hydroxybenzoic acid derivative*	5.8	< 14.9 nmol/mg Creatinine
Benzoic Acid *Glycine N-benzoyltransferase*	<DL	< 488.0 nmol/mg Creatinine
Hippuric Acid *Glycine conjugate of benzoate*	399.0 H	< 291.9 nmol/mg Creatinine

Isoflavone microbial Metabolites	Result	Reference
Equol *Isoflavone metabolite*	11.9	< 12.8 nmol/mg Creatinine

Fungal Assessment	Result	Reference
Arabinitol *Dehydrogenase*	2.1	< 9.0 nmol/mg Creatinine

Indoleacetic Acid:

- A product of tryptophan fermentation.
- If elevated, decrease protein intake and address digestion and GI issues. Bacteroides, Clostridia, and E. coli ferment tryptophan to produced indoleacetic acid. It has been found elevated in liver disease, ASD, and cancer and has been noted as a marker of microbial activity.
- Indoleacetic acid can be degraded by Bacillus subtilis, or Pseudomonas aeruginosa.
- Indoleacetic acid has been found in many foods, such as lettuce, cherry tomato, Chinese bayberry, and okra.
- Supplementation with tryptophan or 5-hydroxy-tryptophan (5HTP) may elevate levels, but a high value does not indicate the need to reduce or eliminate intake.
- Might have some correlation with Hartnup's disease.

CASE STUDY

Hippuric Acid (Hippurate):

- Benzoic acid is metabolized to hippuric acid and excreted. Hippuric acid is a normal urinary metabolite associated with microbial degradation of certain dietary components.
- Levels of hippuric acid rise with the microbial breakdown of chlorogenic acid found with the consumption of fruit juice, tea, and wine, and many fruits and vegetables.
- Though a defect in the enzymatic conjugation of benzoic to hippuric acid has been noted in Crohn's disease patients, research implicates altered gut microbial metabolism as the cause of decreased hippuric acid.

- Other research has found a positive association between Clostridia spp. and hippuric acid levels.
- Hippuric acid has been positively associated with gut diversity.
- If elevated, evaluate benzoic acid and glycine levels.
- Support with glycine if needed.
- A bacterial product of phenylalanine metabolism.
- Higher levels indicate GI bacterial overgrowth.

CASE STUDY

GI-MAP

Opportunistic Bacteria			
Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	**2.34e5**	**High**	<1.50e5
Enterococcus faecalis	**<dl**		<1.00e4
Enterococcus faecium	**2.69e2**		<1.00e4
Morganella spp.	**<dl**		<1.00e3
Pseudomonas spp.	**<dl**		<1.00e4
Pseudomonas aeruginosa	**<dl**		<5.00e2
Staphylococcus spp.	**<dl**		<1.00e4
Staphylococcus aureus	**1.99e3**	**High**	<5.00e2
Streptococcus spp.	**1.69e4**	**High**	<1.00e3
Methanobacteriaceae (family)	**4.99e8**		<5.00e9
Potential Autoimmune Triggers	Result		Normal
Citrobacter spp.	**<dl**		<5.00e6
Citrobacter freundii	**<dl**		<5.00e5
Klebsiella spp.	**<dl**		<5.00e3
Klebsiella pneumoniae	**<dl**		<5.00e4
M. avium subsp. paratuberculosis	**<dl**		<5.00e3
Prevotella spp.	**6.78e7**		<1.00e8
Proteus spp.	**<dl**		<5.00e4
Proteus mirabilis	**<dl**		<1.00e3
Fusobacterium spp.	**2.98e6**		<1.00e8

CASE STUDY

GI-MAP

Intestinal Health		
Digestion	Result	Normal
Steatocrit	**<dl**	<15 %
Elastase-1	**>750**	>200 ug/g
GI Markers	Result	Normal
b-Glucuronidase	**1046**	<2486 U/mL
Occult Blood - FIT	**0**	<10 ug/g
Immune Response	Result	Normal
Secretory IgA	**633**	510 - 2010 ug/g
Anti-gliadin IgA	**47**	0 - 157 U/L
Inflammation	Result	Normal
Calprotectin	**4**	<173 ug/g

ORGANIC METABOLOMICS

A NEW education platform, designed to assist our practitioners with OMX

We understand that the OMX test is very comprehensive and can at times be overwhelming due to the large amount of literature associated with metabolomics. Therefore, DFH have created an interactive LMS platform that enables practitioners to navigate through each section and subsection of the OMX report and obtain comprehensive support for their patients OMX report.

THANK YOU

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